REMARKS/ARGUMENTS

Claims 38-47 are pending.

Claims 38-43 were examined and rejected.

Claims 38-41 and 44 are amended. Support for the amendment is found on page 9, lines 1-2 and page 29, lines 3-5 of the specification.

The Applicants request reconsideration of this application in view of the remarks set forth below.

Specification

The Examiner requests that the status of the priority applications is updated in the first paragraph of the application.

The first paragraph of the application has been amended to update the status of the priority applications.

The Applicants believe that this request has been addressed.

Sequence listing

The specification is objected to for reciting sequences that are not associated with a sequence identifier.

The specification has been amended to include sequence identifiers where appropriate.

The Applicants believe that the specification is now in full compliance with 37 C.F.R. §§ 1.821-1.825.

Rejection of claims under 35 U.S.C. § 112, second paragraph

Claim 38 is rejected under 35 U.S.C. § 112, second paragraph, because it is assertedly unclear whether it is the claimed composition or the Tankyrase H protein that exhibits PARP activity.

Claim 38 has been amended to make it clear that it is the Tankyrase H protein that exhibits PARP activity.

It is believed that this rejection has been adequately addressed. Withdrawal of this rejection is requested.

Claim 39 is rejected under 35 U.S.C. § 112, second paragraph, because the metes and bounds of the term "test agent" are unclear.

Claim 39 has been amended to recite a candidate bioactive agent. As would be clear from the description in the specification at page 28, line 39 to page 30 line 39, candidate bioactive agents are molecules that are to be tested for Tankyrase H modulatory activity.

It is believed that this rejection has been adequately addressed. Withdrawal of this rejection is requested.

Claim 44 is rejected under 35 U.S.C. § 112, second paragraph, because there is insufficient antecedent support for "said cell".

Claim 44 has been amended to make it dependent upon claim 42.

Since claim 42 recites "cells" and claim 44 now recites "said cells", it is believed that this rejection has been adequately addressed.

Withdrawal of this rejection is requested.

Rejection of claims under 35 U.S.C. § 112, first paragraph (new matter)

Claims 38-40 are rejected under 35 U.S.C. § 112, first paragraph, as being drawn to subject matter that is assertedly not described in the application as originally filed. This is a new matter rejection.

The first basis for this rejection is the Examiner's belief that a "non-naturally occurring composition", as recited in claim 38, is not described in the application as originally filed.

Without any intention to acquiesce to the correctness of this rejection and solely to expedite prosecution, claim 38 has been amended to delete the phrase "non-naturally occurring".

The Applicants submit that this rejection has been adequately addressed. Withdrawal of this rejection is respectfully requested.

The second basis for this rejection is the Examiner's belief that a "test agent", as recited in claim 39, is not described in the application as originally filed.

Without any intention to acquiesce to the correctness of this rejection and solely to expedite prosecution, claim 39 has been amended to recite a "candidate bioactive agent".

Since candidate bioactive agents are fully supported on page 29, lines 3-10, it is believed that this rejection has been adequately addressed. Withdrawal of this rejection is respectfully requested.

Rejection of claims under 35 U.S.C. § 112, first paragraph (enablement)

Claims 38-44 are rejected under 35 U.S.C. § 112, first paragraph, as being drawn to subject matter that is assertedly not enabled by the specification as originally filed.

The Office Action bases this rejection on the idea that the specification does not give adequate guidance on which amino acids of the claimed Tankyrase H protein could be changed without changing the function of the protein. The Applicants respectfully disagree.

The law regarding enablement of inventions is clear: "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation."[1]

The Examiner is respectfully reminded that the scope of enablement must only bear a "reasonable correlation" to the scope of the claims (MPEP §2164.08) and the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled (MPEP §2164.08(b)). The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort that is normally required in the art (MPEP §2164.08(b)).

The specification describes Tankyrase H molecules has having "PARP", i.e., poly-ADP ribose polymerase, activity. The specification describes two isoforms of Tankyrase H molecules having PARP activity (SEQ ID NOS:3 and 4) and describes two different Tankyrase H variants that do not have PARP activity (see Fig. 5). The two isoforms of Tankyrase H molecules recited by sequence have a "PARP domain" (see Fig. 5), which is a well known domain. In fact, a search of Medline using the search strategy ("parp" OR "poly-ADP ribose polymerase") yielded 1,561 matches among references published in 1999 alone (the year of the earliest priority application), and, as such, the Applicants respectfully submit that the general state of the art with respect to PARP domain-containing proteins is exceedingly high.

Further, with respect to PARP domain proteins, NCBI's "conserved domain database" indicates that there are at least about 70 examples of eukaryotic PARP domain polypeptides other than the ones provided in SEQ ID NOS:3 and 4 (see Exhibit A). Exhibit B is an alignment of six exemplary eukaryotic

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[1] *United States v. Telectronics, Inc.*, 8 USPQ 2d 1217, 1233 (Fed. Cir. 1988), *cert. denied*, 490 U.S. 1046 (1989). See also *Genentech, Inc. v. Novo Nordisk*, 42 USPQ 2d 1001 (Fed. Cir. 1997), *cert. denied*, 522 U.S. 963 (1997); *Scripps Clinic and Research Foundation v. Genentech, Inc.*, 18 USPQ 2d 1001 (Fed. Cir. 1991).

PARP domains indicating that some amino acids are highly conserved in the PARP domain, whereas other amino acids are highly variable.

Further, the crystal structure of the catalytic domain of poly(AD-ribose) polymerase is known (e.g. Ruf et al., Proc Natl Acad Sci U S A. 1996 93:7481-5; abstract enclosed as Exhibit C), and the structure/function relationship between the amino acids of PARP domains has been studied extensively (e.g. Uchida et al., Gene. 1993 137:293-7 and Masson, Biochimie. 1995 77:456-61; abstracts enclosed as Exhibits D and E, respectively). In fact, the PARP domain has been extensively mutagenized to reveal particular amino acids of importance for PARP activity (Simonin, J Biol Chem. 1993 268:8529-35 and Rolli, Biochemistry 1997 36:12147-54; abstracts enclosed as Exhibits F and G, respectively).

The Applicants respectfully submit that in view of the above information, a skilled person would know exactly which amino acids of SEQ ID NOS:3 or 4 cannot be changed, and others that could be changed, in order to create a variant that retains PARP activity.

In summary, the specification discloses that the instant tankyrase is a PARP domain protein and describes two tankyrase H proteins that have PARP activity and two tankyrase H variants that do not have PARP activity. The level of knowledge of the structure of PARP domain proteins is, in general, extremely high, and, as such, a skilled person, upon viewing the sequence of SEQ ID NOS:3 or 4, would be able to predict, with a high degree of certainty, which amino acids of SEQ ID NOS:3 or 4 could be changed without altering the PARP activity of the polypeptide and practice the claimed subject matter without undue experimentation.

In view of the foregoing discussion, withdrawal of this rejection is respectfully requested.

Rejection of claims under 35 U.S.C. § 112, first paragraph (written description)

Claims 38-44 are rejected under 35 U.S.C. § 112, first paragraph, as being drawn to subject matter that is assertedly inadequately described by the specification as originally filed.

In making the rejection, the Office Action argues that "The specification does not contain any disclosure of the structure of **all** the polypeptide sequence derived from SEQ ID NO:3 or 4, including fragments and variants within the scope of the claimed genus." (emphasis added). Further, the Office Action refers the Applicant to the revised guidelines concerning compliance with the written description requirement of 35 U.S.C. §112, ¶1.

With respect to satisfying the written description requirement, even in an "unpredictable art," applicants "are *not* required to disclose *every* species encompassed by their claims . . . ."[2] Otherwise, to claim a genus, every species within a genus would have to be explicitly described. This is **not** the law. In other words, the written description requirement does not require a specific description of every species encompassed by a claim.

As such, the Office's argument that the specification does not contain any disclosure of the structure of **all** the polypeptide sequences that are 95% identical to SEQ ID NO:3 or 4, has no bearing on the instant claims because such a level of disclosure is not required by law.

With respect to the written description guidelines, the guidance set forth in the "Synopsis of Application of Written Description Guidelines", as published to the world wide website of the U.S.P.T.O. on March 1st, 2000 (http://www.uspto.gov/web/offices/pac/writtendesc.pdf), indicates that the claims are adequately described.

Example 14 of the Synopsis describes a scenario that is very similar to that currently under examination. Example 14 provides an example of a specification that discloses the sequence of a polypeptide having the sequence of SEQ ID NO:3, and also discloses that the polypeptide has a certain enzymatic activity. This example also states that the specification also "contemplates but does not exemplify" variants of SEQ ID NO:3, and provides an assay for measuring the activity of the protein. In this example, the claims are directed to polypeptides having a sequence that is at least 95% identical to that of SEQ ID NO: 3 and catalyze the reaction of A→B.

The Synopsis states that the claimed subject matter is adequately described by the specification and the requirements of 35 U.S.C. §112 first paragraph have been met because "The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity.

For the Examiner's convenience, Example 14 of the Synopsis of Application of Written Description Guidelines is attached hereto as Exhibit H.

The Applicants respectfully submit that the fact pattern of the example set forth above is very similar to the instant fact pattern. In other words, the instant specification: a) describes the sequence of full length polypeptides (to be more exact, SEQ ID NO:3, SEQ ID NO:4, and two variants shown in Fig.

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[2] *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. (BNA) 214, 218, (C.C.P.A. 1976).

5), b) describes that SEQ ID NO:3 and SEQ ID NO:4 have PARP activity, c) "contemplates but does not exemplify" variants of SEQ ID NOS:3 and 4, and d) provides detailed methods of how PARP activity can be assayed.

As such, by the reasoning set forth in the Example 14 of the Synopsis, in combination with the vast amount of public knowledge on the structure of PARP proteins (discussed in the "enablement" section above), the instant claims should be considered adequately described by the specification, meeting the requirements of 35 U.S.C. §112, first paragraph.

In view of the foregoing discussion, this rejection may be withdrawn.

Rejection of claims under 35 U.S.C. § 102

Claims 38-40 and 42 are rejected under 35 U.S.C. § 102(b), as allegedly anticipated by Simonin (J. Biol. Chem. 1993 268: 8529-8535).

Without any intention to acquiesce to the correctness of this rejection, the claims have been amended to recite a polypeptide that has an amino acid sequence that is at least 95% identical to SEQ ID NO:3 or SEQ ID NO:4.

The polypeptide investigated by Simonin is human PARP1. Since human PARP1 has an amino acid sequence that is less than 95% identical to SEQ ID NO:3 or SEQ ID NO:4, Simon does not disclose each and every element of the rejected claims.

The Applicants submit that this rejection has been adequately addressed. Withdrawal of this rejection is respectfully requested.

Rejection of claims under 35 U.S.C. § 103

Claims 41 and 43-44 are rejected under 35 U.S.C. § 103(a), as allegedly obvious over Simonin in view of Smith (Science 1998 282: 1484-1486).

As established above, Simonin is deficient because it does not teach or suggest a polypeptide that has an amino acid sequence that is at least 95% identical to SEQ ID NO:3 or SEQ ID NO:4.

Like Simonin's PARP protein, Smith's PARP protein also has an amino acid sequence that is less than 95% identical to SEQ ID NO:3 or SEQ ID NO:4.

As such, the combination of Simonin and Smith fails to teach of suggest an element of the rejected claims, i.e., a polypeptide that has an amino acid sequence that is at least 95% identical to SEQ ID NO:3 or SEQ ID NO:4.

The Applicants submit that this rejection has been adequately addressed. Withdrawal of this rejection is respectfully requested.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number RIGL-010CIP3.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: 8/28/06

By: _____
James S. Keddie, Ph.D.
Registration No. 48,920

Enclosures: Exhibits A-H

BOZICEVIC, FIELD & FRANCIS LLP
1900 University Avenue, Suite 200
East Palo Alto, California 94303
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

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